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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|-----------------|-------------|----------------------|---------------------|------------------|
| 10/019,494 | 03/08/2002 | Samuel D. Bernal | 65879-5006 | 1407 |

24574 7590 05/04/2007
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EXAMINER

EBRAHIM, NABILA G

| ART UNIT | PAPER NUMBER |
|----------|--------------|
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1618

| MAIL DATE | DELIVERY MODE |
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05/04/2007

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/019,494

Applicant(s)

BERNAL ET AL.

Examiner

Nabila G. Ebrahim

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 12 December 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1, 2, and 11-20 is/are pending in the application.
- 4a) Of the above claim(s) 2 and 11-20 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

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DETAILED ACTION

The office action dated 2/16/07 is herein vacated.

Election/Restrictions

1. Restriction is required under 35 U.S.C. 121 and 372.

This application contains the following inventions or groups of inventions, which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In accordance with 37 CFR 1.499, applicant is required, in reply to this action, to elect a single invention to which the claims must be restricted.

Group I, claim(s) 1, drawn to a diagnostic method.

Group II, claim(s) 2, drawn to a method for selective killing of oral epithelial cancer.

Group III, claim(s) 11-16, drawn to a composition for selective killing of epithelial cancer cells.

Group IV, claim(s) 17, drawn to a composition for the selective killing of epithelial cancer cells.

Group V, claim(s) 18 and 20, drawn to a method for improved the selective killing of cancerous epithelial cells using the composition of claim 11.

Group VI, claim(s) 19 and 20, drawn to a method for improved the selective killing of cancerous epithelial cells using the composition of claim 17.

2. The inventions listed as Groups III-VI do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: The claims are drawn to compositions and methods that are used as therapeutic means for epithelial cell in general while Groups I, and II are related to methods of diagnosis and selective killing of oral epithelium only. Accordingly, the special technical feature of handling the oral mucosa is not met in Groups III-VI since the body includes many different sites of epithelial cells such as the skin for example.

3. This application contains claims directed to more than one species of the generic invention. These species are deemed to lack unity of invention because they are not so linked as to form a single general inventive concept under PCT Rule 13.1.

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The species are as follows: Applicant is required to elect one of the following species (a, b, or c)

- a. Species in claim 12, and 13, Oxazine and thiazine dyes.
- b. Species in claim 14, alcian blue, malachite green, pheosafranin, acriflavine, pyronin Y, toluylene blue, and brilliant green.
- c. Species in claim 15, peonidin, oxythiamine, teimonium iodine, elliptinium acetate, and furazolium chloride.

Applicant is required, in reply to this action, to elect a single species to which the claims shall be restricted if no generic claim is finally held to be allowable. The reply must also identify the claims readable on the elected species, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered non-responsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species.

MPEP § 809.02(a).

4. The claims are deemed to correspond to the species listed above in the following manner:

Claims 11, 12, 13, and 16,
Claims 11, 14, and 16, or
Claims 11, 15, and 16.

The following claim(s) are generic: 11.

5. The species listed above do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, the species lack the same or corresponding

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special technical features for the following reasons: the species are different compounds having different properties and different chemical structure.

6. During a telephone conversation with Mr. Brennan Swain on 2/28/2007 a provisional election was made without traverse to prosecute the invention of Group I, claim

1. Affirmation of this election must be made by applicant in replying to this Office action.

Claims 2, 11-20 are withdrawn from further consideration by the examiner, 37

CFR 1.142(b), as being drawn to a non-elected invention.

7. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Pomerantz

Edwin WO 9726018.

Pomerantz teaches in vivo detection (corresponds to step b of claim 1) of oral premalignant lesions and oral carcinomas, including the steps of sequentially rinsing (corresponds to step a of claim 1) the oral cavity with a dye stain composition which is selectively retained by cancerous and precancerous tissues, and a rinse composition for

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removing unretained stain composition, the step of applying to oral tissue, a stain composition comprising a non-toxic dye other than toluidine blue 0 (claim 1). Pomerantz also disclosed that this type of staining is dependent on the dye gaining access to internal subcellular structures such as the nucleus. Such access is readily obtained only by "fixing" a tissue sample of formaldehyde or other reagent that disrupts the cellular membrane without destroying general cellular structure (page 2, line 26 bridging to page 3, line 4). Note that it is expected that the mitochondria as a subcellular structure would at least partially absorb the dye. It is also known that the disclosure of oral carcinomas means oral malignancy of epithelial cells recited in instant claim 1.

In addition, Pomerantz teaches that in-vivo diagnostic procedures for detection of premalignant oral lesions or oral carcinomas, employing dye compositions, which are selectively retained by tissues rendered abnormal due to dysplasia, hyperplasia, tumorigenesis, and other active surface lesions, are known in the art.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37

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CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claim 1 is rejected under 35 U.S.C. 103(a) as being unpatentable over Pomerantz Edwin WO 9726018 in view of Oseroff et al., Intramitochondrial Dyes Allow Selective in vitro Photolysis of Carcinoma Cells, PNAS, December 15, 1986, vol. 83, no. 24, 9729-9733. (hereinafter Oseroff)

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Pomerantz has been discussed above.

Pomerantz did not teach explicitly that the mitochondria is the subcellular structure that will be marked by the dye.

Oseroff teaches that carcinoma cell mitochondria preferentially accumulate and retain cationic dyes to a much greater extent than most normal cells.

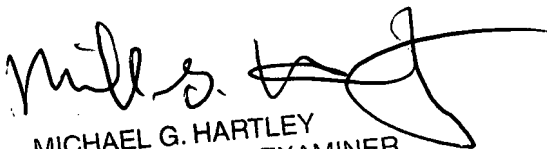
Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to use a non-toxic dye other than toluidine blue 0 to mark premalignant carcinoma cells as Pomerantz teaches to target the mitochondria that will be marked because Oseroff teaches that mitochondria in carcinomatous cells can absorb cationic dyes to a much greater extent than normal cells. The expected result would be a method to detect cancerous cells of the oral epithelium in vivo.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nabila G. Ebrahim whose telephone number is 571-272-8151. The examiner can normally be reached on 8:00AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Hartley can be reached on 571-272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Nabila Ebrahim
3/9/07


MICHAEL G. HARTLEY
SUPERVISORY PATENT EXAMINER